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Pneumocystis Infection

Pneumocystis pneumonia, although a rare disease in this country, has become a serious and widespread infection among young infants in many Central European countries during the past forty years. Although the majority have been sporadic cases, several small epidemics have occurred among infants in nurseries and hospitals in some of which temporary closure of the institution has been necessary.

The clinical course and pathology of the disease had been recognized for many years but the ætiology remained unsolved until van der Meer & Brug (1942) were able to demonstrate *Pneumocystis carinii* in impression smears taken from human lungs. Later Vanek (1951) in Czechoslovakia demonstrated the causative parasite in the intra-alveolar exudate in lung sections shortly after the introduction of the PAS staining method.

The causative organism *Pneumocystis carinii* was originally discovered by Chagas (1909) in the lung of a rat and he mistook it for a stage in the life-cycle of *Trypanosoma cruzii*. In 1912 the parasite was given its present name by Delanöe & Delanöe. Wenyon (1926) classified *P. carinii* as a protozoon placing it in the Class Sporozoa, and although it is still regarded as such by the majority of parasitologists, others, notably Csillag & Brandstein (1954), considered it should be classed as a fungus and placed among the Saccharomycetes.

Pneumocystis pneumonia is an infection which is still endemic in Germany, Poland, Scandinavia, Switzerland and Hungary, though fewer cases are now seen in some of these countries than formerly. In recent years an increasing number of cases have been recognized in North America and small epidemics and sporadic cases have been described in Chile, Australasia and Great Britain. Among the first cases discovered in this country was that described by Baar (1955).

The distinctive chronic interstitial pneumonia, resembling that seen in congenital syphilis, was described by Rössle (1923), and further accounts describing the clinical course of the illness and the pathological changes were given by Ammich (1938) and Benecke (1938). The importance of the disease in endemic areas may be judged from the statement made by Deamer & Zollinger (1953) that in Switzerland over 700 cases had occurred and that the incidence was higher in neighbouring countries.

The disease affects mainly infants, and especially premature infants, during the first six months, and the incubation period is about six weeks. Clinically the illness is characterized by increasing shortness of breath, cyanosis, very little cough, an absence of pyrexia and a normal white cell count in the blood. In several instances the infants have displayed hypo- or agamma-globulinæmia associated with hypoplasia of the lymphoid tissue. Radiologically, the lungs present numerous opacities at an early stage in the illness.

Although predominantly an infection contracted in infancy, an increasing number of cases is being reported in adults and children mainly as a terminal complication of leukæmia, malignant lymphomatous states and in advanced forms of malignant disease. In almost every instance the diagnosis has only been established after death. Pneumocystis infection may also complicate steroid therapy, occurring during the withdrawal of the drugs following a prolonged course of treatment. It has recently been described in a series of patients who died following unsuccessful renal grafting operations (Rifkind *et al.* 1964). In these patients the natural body immune responses had been artificially and purposely reduced to allow successful acceptance of the grafted tissue. In the majority of both the infant and adult pneumocystis infections the natural body immune mechanisms have probably been diminished by immaturity, disease or artificial means and therefore this type of infection qualifies for inclusion among the 'opportunistic' infections.

Macroscopically, the lungs contain extensive pale, greyish-yellow or pinkish, firm, consolidated areas with normal intervening lung tissue and overlying pleura. The consolidated tissue often resembles pancreatic tissue and the septal tissues are prominent and thickened.

Microscopically, there is extensive chronic inflammatory cell infiltration of all the interstitial planes of the lung with lymphocytes and plasma cells. Fibrosis is absent but the alveolar epithelium is often hyperplastic and hyaline membranes may be found. The majority of the alveoli are filled with a foamy, eosinophilic, structureless exudate

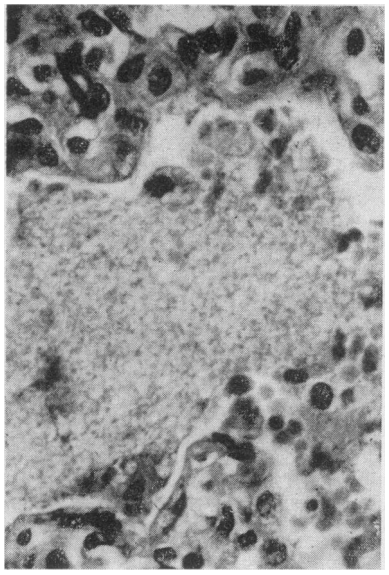

Fig 1 *H & E stained section showing foamy exudate filling alveolar spaces. No cysts of* Pneumocystis carinii *and very few cells can be seen.* × *355*

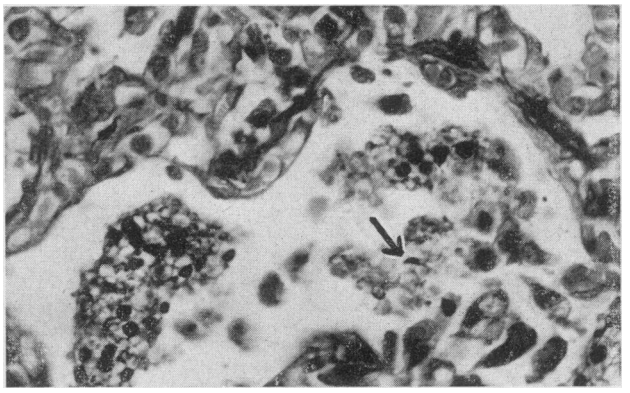

Fig 2 *Silver-methenamine-stained section to show intra-alveolar exudate containing black rounded bodies which are cysts of* P. carinii. *One crescentic form can be seen (arrowed) near the centre of the picture.* × *355*

containing very few cells (Fig 1). Impression smears of the exudate, if stained with Giemsa, often reveal the causative organism. The pneumocysts are best demonstrated in tissue sections by the silver methenamine stains (Fig 2), although they were first shown by the PAS stain. The latter method shows the intracystic chromatin particles which cannot be seen in the silver-stained parasite.

Although the mortality rate in infants reaches to 40–50%, some cases recover while others pursue a chronic course during which the intra-alveolar exudate may become calcified inducing a foreign-body giant-cell reaction.

The electron microscopic structure of the pneumocysts was investigated by Wessel & Ricken (1958) and Bommer (1962). Each cyst consists of a thick transparent outer cyst wall surrounding a membranous structure that in-pouches to enclose chromatin particles between the membrane and the inner surface of the cyst wall. Up to about 6 chromatin particles may be found within each cyst. After extrusion of the particles the cyst collapses to assume a crescentic shape, and may be readily recognized in the silver-methenamine-stained sections examined by light microscopy.

Pneumocystis infections may co-exist with other forms of 'opportunistic' infections, particularly cytomegalic inclusion-body pneumonia and occasionally with fungus infections. Cytomegalic inclusion-body pneumonia occurs with pneumocystis infections in both infants and adults although generalized infections involving the lungs in adults are normally rare. The cytomegalic inclusion-body infection is thought to start in fœtal life and antedates the onset of pneumocystic pneumonia which is a post-natal infection.

P. carinii has so far not been found to occur in man outside the lung and the source of the infections is unknown. It has never yet been cultured successfully outside the body although experimental infections have been induced in newborn mice, in young scorbutic guinea-pigs and in cortisone-treated rats.

Pneumocysts have very seldom been discovered in sputum during life and this, combined with the absence of any reliable laboratory diagnostic test, makes the ante-mortem diagnosis entirely dependent on the recognition of the clinical and radiological changes. In about one-sixth of all cases there may be a rise in the cold agglutinins in the blood which can lead to a mistaken diagnosis of atypical virus pneumonia due to the Eaton agent.

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Dr R W Riddell (*Department of Bacteriology, Brompton Hospital, London*) read a paper entitled **Fungal Infections Complicating Existing Disease**